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EXAMINER
GORDON, BRIAN R

ART UNIT	PAPER NUMBER
1743	11

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/846,474	Applicant(s) BASS, JAY K.	
	Examiner Brian R. Gordon	Art Unit 1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *40-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *06 May 2003* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). *5* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

1. The information disclosure statement (IDS) submitted on May 6, 2003 was considered by the examiner.

Specification

1. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Drawings

2. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on May 6, 2003 have been approved. A proper drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The correction to the drawings will not be held in abeyance.

Response to Arguments

3. Applicant's arguments with respect to claims 1-39 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, 5-7, 9-11, 20, 25, 27, 31-32, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. US 6,024,925 in view of Bogen et al. US 6,541,261.

Little et al. discloses parallel dispensing tools that can deliver defined and controlled volumes of fluid to generate multi-element arrays of sample material on a substrate surface. The substrates surfaces can be flat or geometrically altered to include wells of receiving material. FIG. 1 depicts a system 10 that includes a data

processor 12, a motion controller 14, a robotic arm assembly 16, a monitor element 18A, a central processing unit 18B, a microliter plate of source material 20, a stage housing 22, a robotic arm 24, a stage 26, a pressure controller 28, a conduit 30, a mounting assembly 32, a pin assembly 38 (dispense head with multiple dispensers), and substrate elements 34. The interior chamber can be connected to a pressure source that will control the pressure within the interior chamber to regulate the flow of fluid within the interior chamber of the pins (different dispensers). In the view shown by FIG. 1, it is also illustrated that the robotic assembly 16 can include a moveable mount element 40 and a horizontal slide groove 42. The robotic arm 24 can optionally pivot about a pin 36 to increase the travel range of the arm 24 so that arm 24 can dispose the pin assembly 38 above the source plate 20. The data processor 12 depicted in FIG. 1 can be a conventional digital data processing system such as an IBM PC compatible computer system that is suitable for processing data and for executing program instructions that will provide information for controlling the movement and operation of the robotic assembly 16. It will be apparent to one skilled in the art that the data processor unit 12 can be any type of system suitable for processing a program of instructions signals that will operate the robotic assembly 16. Optionally the data processor 12 can be a micro-controlled assembly that is integrated into the robotic housing 16. In further alternative embodiments, the system 10 need not be programmable and can be a single board computer having a firmware memory for storing instructions for operating the robotic assembly 16. In the embodiment depicted in FIG. 1, there is a controller 14 that electronically couples between the data processor

12 and the robotic assembly 16. The depicted controller 14 is a motion controller that drives the motor elements of the robotic assembly 16 for positioning the robotic arm 24 at a selected location. Additionally, the controller 14 can provide instructions to the robotic assembly 16 to direct the pressure controller 28 to control the volume of fluid ejected from the individual pin elements of the depicted pin assembly 38. The depicted robotic assembly 16 is a gantry system that includes an XY table for moving the robotic arm about an XY plane, and further includes a Z axis actuator for moving the robotic arm orthogonally to that XY plane.

FIG. 6A is a piezo electric transducer element which forms around the parameter of the capillary 112 and can transform an electrical pulse received from the pulse generator within a robotic assembly 16 to cause fluid to eject from the orifice 118 of the capillary 112.

After depositing the sample arrays onto the surface of the substrate, the arrays can be analyzed (detection of drops) using any of a variety of means (e.g., spectrometric techniques, such as UV/IVIS, IR, fluorescence, chemiluminescence, NMR spectroscopy or mass spectrometry).

The matrix drops were observed by employing visualization via a CCD camera (capturing an image of drops) (column 16, lines 56-65).

Little et al. discloses methods for rapidly analyzing sample materials. To this end sample arrays can be formed on a substrate surface according to any of the techniques discussed above. The sample arrays are then analyzed by mass spectrometry to collect spectra data that is representative of the composition of the samples in the array. It is

understood that the above methods provide processes that allow for rapidly dispensing definite and controlled volumes of analyte material. In particular these processes allow for dispensing sub to low nanoliter volumes of fluid. These low volume deposition techniques generate sample arrays well suited for analysis by mass spectrometry. For example, the low volumes yield reproducibility of spot characteristics, such as evaporation rates and reduced dependence on atmospheric conditions such as ambient temperature and light.

Continuing with the example shown in FIG. 1, the arrays can be prepared by loading oligonucleotides (0.1-50 ng/lll) of different sequences or concentrations into the wells of a 96 well microtiter source plate 20; the first well can be reserved for holding a matrix solution. A substrate 34, such as a pitted silicon chip substrate, can be placed on the stage 26 of the robotics assembly 16 and can be aligned manually to orient the matrix of wells about a set of reference axes. The control program executing on the data processor 12 can receive the coordinates of the first well of the source plate 20. The robotic arm 24 can dip the pin assembly 38 into source plate 20 such that each of the 16 pins is dipped into one of the wells. Each vesicle can fill by capillary action so that the full volume of the holding chamber contains fluid. Optionally, the program executing on the data processor 12 can direct the pressure controller to fill the interior chamber 58 of the pin assembly 38 with a positive bias pressure that will counteract, in part, the force of the capillary action to limit or reduce the volume of fluid that is drawn into the holding chamber.

Optionally, the pin assembly 38 can be dipped into the same 16 wells of the source plate 20 and spotted on a second target substrate. This cycle can be repeated on as many target substrates as desired. Next the robotic arm 24 can dip the pin assembly 38 in a washing solution, and then dip the pin assembly into 16 different wells of the source plate 20, and spot onto the substrate target offset a distance from the initial set of 16 spots. Again this can be repeated for as many target substrates as desired. The entire cycle can be repeated to make a 2X2 array from each vesicle to produce an 8X8 array of spots (2X2 elements/vesicle X 16 vesicles=64 total elements spotted).

In an alternative practice of the invention, oligonucleotides of different sequences or concentrations can be loaded into the wells of up to three different 384-well microtiter source plates; one set of 16 wells can be reserved for matrix solution. The wells of two plates are filled with washing solution. Five microtiter plates can be loaded onto the stage of the robotic assembly 16. A plurality of target substrates can be placed abutting an optional set of banking or registration pins disposed on the stage 26 and provided for aligning the target substrates along a set of reference axes. If the matrix and oligonucleotide are not pre-mixed, the pin assembly can be employed to first spot matrix solution on all desired target substrates. In a subsequent step the oligonucleotide solution can be spotted in the same pattern as the matrix material to re-dissolve the matrix. Alternatively, a sample array can be made by placing the oligonucleotide solution on the wafer first, followed by the matrix solution, or by-pre-mixing the matrix and oligonucleotide solutions.

After depositing the sample arrays onto the surface of the substrate, the arrays can be analyzed using any of a variety of means (e.g., spectrometric techniques, such as UV/IVIS, IR, fluorescence, chemiluminescence, NMR spectroscopy or mass spectrometry). For example, subsequent to either dispensing process, sample loaded substrates can be placed onto a MALDI-TOF source plate and held there with a set of beveled screw mounted polycarbonate supports. In one practice, the plate can be transferred on the end of a probe to be held onto a 1 □m resolution, 1" travel xy stage (Newport) in the source region of a time-of-flight mass spectrometer. It will be apparent to one of ordinary skill in the art that any suitable mass spectrometry tool can be employed with the present invention without departing from the scope thereof.

Little et al. does not disclose that he dispensed liquid is detected "at" (as defined by applicant) respective locations on the substrate.

Bogen et al. disocloses an automated slide stainer with slides mounted in a horizontal position on a rotary carousel. Reagents and rinse liquids are automatically dispensed onto tissue sections or cells mounted on slides for the purpose of performing chemical or immunohistochemical stains.

The device comprise a dispense sensor 95 is positioned underneath the bulk liquid dispensing port 68 to provide verification that liquid was dispensed when one of the solenoid valves 72a-72f were transiently opened. The dispense sensor 95 comprises an optical sensor and an LED light source. When liquid is dispensed from the bulk liquid dispensing port 68, the liquid interrupts the light beam. The change in

resistance across the sensor as a result of the decrement in light intensity is communicated to the controller 86.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify method and the device of Little et al. to include the drop sensing element as taught by Bogen in order to allow for inventory of the fluid dispensed and monitor if the dispensers are functioning correctly.

2. Claims 1-2, 6, 12, 18, 20, 25, 27, 31-32, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalon et al. US 6,110,426 in view of Bogen et al. US 6,541,261.

Shalon et al. disclose method and apparatus for forming microarrays of biological samples on a support.

In one embodiment, the surface is glass slide surface coated with a polycationic polymer, such as polylysine, and the biopolymers are polynucleotides. In another embodiment, the substrate has a water-impermeable backing, a water-permeable film formed on the backing, and a grid formed on the film. The grid is composed of intersecting water-impervious grid elements extending from said backing to positions raised above the surface of said film, and partitions the film into a plurality of water-impervious cells. A biopolymer array is formed within each well.

More generally, there is provided a substrate for use in detecting binding of labeled polynucleotides to one or more of a plurality different-sequence, immobilized polynucleotides. The substrate includes, in one aspect, a glass support, a coating of a

polycationic polymer, such as polylysine, on said surface of the support, and an array of distinct polynucleotides electrostatically bound non-covalently to said coating, where each distinct biopolymer is disposed at a separate, defined position in a surface array of polynucleotides.

Shalon also discloses a method of forming a microarray of analyte-assay regions on a solid support or substrate, where each region in the array has a known amount of a selected, analyte-specific reagent.

FIG. 1 illustrates, in a partially schematic view, a reagent-dispensing device 10 useful in practicing the method. The device generally includes a reagent dispenser 12 having an elongate open capillary channel 14 adapted to hold a quantity of the reagent solution, such as indicated at 16, as will be described below. The capillary channel is formed by a pair of spaced-apart, coextensive, elongate members 12a, 12b which are tapered toward one another and converge at a tip or tip region 18 at the lower end of the channel. More generally, the open channel is formed by at least two elongate, spaced-apart members adapted to hold a quantity of reagent solutions and having a tip region at which aqueous solution in the channel forms a meniscus, such as the concave meniscus illustrated at 20 in FIG. 2A. The advantages of the open channel construction of the dispenser are discussed below.

With continued reference to FIG. 1, the dispenser device also includes structure for moving the dispenser rapidly toward and away from a support surface, for effecting deposition of a known amount of solution in the dispenser on a support. In the

embodiment shown, this structure includes a solenoid 22 which is activatable to draw a solenoid piston 24 rapidly downwardly, then release the piston, e.g., under spring bias, to a normal, raised position, as shown. The dispenser is carried on the piston by a connecting member 26, as shown. The just-described moving structure is also referred to herein as dispensing means for moving the dispenser into engagement with a solid support, for dispensing a known volume of fluid on the support.

The solid support containing the microarrays are detected and analyzed as a single sheet of material using standard radioactive, fluorescent, or colorimetric detection mean.

Shalon et al. do not disclose that he dispensed liquid is detected "at" (as defined by applicant) respective locations on the substrate.

Bogen et al. disoclose an automated slide stainer with slides mounted in a horizontal position on a rotary carousel. Reagents and rinse liquids are automatically dispensed onto tissue sections or cells mounted on slides for the purpose of performing chemical or immunohistochemical stains.

The device comprise a dispense sensor 95 is positioned underneath the bulk liquid dispensing port 68 to provide verification that liquid was dispensed when one of the solenoid valves 72a-72f were transiently opened. The dispense sensor 95 comprises an optical sensor and an LED light source. When liquid is dispensed from the bulk liquid dispensing port 68, the liquid interrupts the light beam. The change in resistance across the sensor as a result of the decrement in light intensity is communicated to the controller 86.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify method and the device of Shalon et al. to include the drop sensing element as taught by Bogen in order to allow for inventory of the fluid dispensed and monitor if the dispensers are functioning correctly.

Although Shalon et al. disclose that the substrate is coated, it would have been obvious to one of ordinary skill in the art to recognize that the array may be fabricated by applying the coating to selected locations.

3. Claims 8-11, 13-14, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Little et al. in view of Bogen et al. US 6,541,261 as applied to claims 1-2, 5-7, 9-11, 20, 25, 27, 31-32, and 38-39 above, and further in view of Wilhelm et al. US 5,715,327.

Little et al. in view of Bogen et al. do not recite that the substrate is detected for an error.

Wilhelm et al. US 5,715,327 disclose a method and apparatus for determining whether a slide is suitable for processing. A suite of suitability tests are performed by an automated microscope system. The tests include magnification error flags, staining flags, and main optical density flags. Slide suitability score results from analyses applied to measurements of a slide's characteristics and an automated cytology system's effectiveness.

FIGS. 1A, 1B and 1C show a schematic diagram of one embodiment of the apparatus of the invention for field of view prioritization. The apparatus of the invention

comprises an imaging system 502, a motion control system 504, an image processing system 536, a central processing system 540, and a workstation 542. The imaging system 502 is comprised of an illuminator 508, imaging optics 510, a CCD camera 512, an illumination sensor 514 and an image capture and focus system 516. The image capture and focus system 516 provides video timing data to the CCD cameras 512, the CCD cameras 512 provide images comprising scan lines to the image capture and focus system 516. An illumination sensor intensity is provided to the image capture and focus system 516 where an illumination sensor 514 receives the sample of the image from the optics 510. In one embodiment of the invention, the optics may further comprise an automated microscope 511. The illuminator 508 provides illumination of a slide. The image capture and focus system 516 provides data to a VME bus 538. The VME bus distributes the data to an image processing system 536. The image processing system 536 is comprised of field-of-view processors 568. The images are sent along the image bus 564 from the image capture and focus system 516. A central processor 540 controls the operation of the invention through the VME bus 538. In one embodiment the central processor 562 comprises a MOTOROLA 68030 (TM) CPU. The motion controller 504 is comprised of a tray handler 518, a microscope stage controller 520, a microscope tray controller 522, and a calibration slide 524. The motor drivers 526 position the slide under the optics. A bar code reader 528 reads a barcode located on the slide 524. A touch sensor 530 determines whether a slide is under the microscope objectives, and a door interlock 532 prevents operation in case the doors are open. Motion controller 534 controls the motor drivers 526 in response to the central

processor 540. An Ethernet communication system 560 communicates to a workstation 542 to provide control of the system. A hard disk 544 is controlled by workstation 550. In one embodiment, workstation 550 may comprise a SUN SPARC CLASSIC (TM) workstation. A tape drive 546 is connected to the workstation 550 as well as a modem 548, a monitor 552, a keyboard 554, and a mouse pointing device 556. A printer 558 is connected to the ethernet 560.

During slide suitability testing, the central computer 540, running a real time operating system, controls the microscope 511 and the processor to acquire and digitize images from the microscope 511. The flatness of the slide may be checked, for example, by contacting the four corners of the slide using a computer controlled touch sensor. The computer 540 also controls the microscope 511 stage to position the specimen under the microscope objective, and from one to fifteen field of view (FOV) processors 568 which receive images under control of the computer 540.

Software may be embedded, for example, in the central processor 540. The processor 540 computes a suitability score that indicates whether a slide passed or failed.

It would have been obvious to one of ordinary skill in the art to modify the or method of Little by employing the method of Wilhelm et al. to detect an error in deposition to the substrate or determine the suitability of the substrate.

4. Claims 1-2, 6, 12, 18, 20, 25, 27, 31-32, and 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz et al. US 6,346,290 in view of Bogen et al. US 6,541,261.

Schultz et al. disclose methods and apparatus for the preparation and use of a substrate having an array of diverse poltmetric materials in predefined regions thereon. A substrate having an array of diverse materials thereon is generally prepared by delivering components of materials to predefined regions on a substrate, and simultaneously reacting the components to form at least two materials.

In one embodiment of the invention, a first component of a first material is delivered to a first region on a substrate, and a first component of a second material is delivered to a second region on the same substrate. Thereafter, a second component of the first material is delivered to the first region on the substrate, and a second component of the second material is delivered to the second region on the substrate. **The process is optionally repeated**, with additional components, to form a vast array of components at predefined, i.e., known, locations on the substrate. Thereafter, the components are simultaneously reacted to form at least two materials. The components can be sequentially or simultaneously delivered to predefined regions on the substrate in any stoichiometry, including a gradient of stoichiometries, using any of a number of different delivery techniques.

In the delivery systems of the present invention, a small, precisely metered amount of each reactant component is delivered into each reaction region. This may be accomplished using a variety of delivery techniques, either alone or in combination with a variety of masking techniques. For example, thin-film deposition in combination with physical masking or photolithographic techniques can be used to deliver various reactants to selected regions on the substrate. The various reactant components can be

deposited into the reaction regions of interest from a dispenser in the form of droplets or powder. Suitable dispensers include, for example, micropipettes, mechanisms adapted from ink-jet printing technology, or electrophoretic pumps.

Once the components of interest have been delivered to predefined regions on the substrate, they can be reacted using a number of different synthetic routes to form an array of materials The components can be reacted using, for example, solution based synthesis techniques, photochemical techniques, polymerization techniques, template directed synthesis techniques, epitaxial growth techniques, by the sol-gel process, by thermal, infrared or microwave heating, by calcination, sintering or annealing, by hydrothermal methods, by flux methods, by crystallization through vaporization of solvent, etc. Thereafter, the array can be screened (detected "on" the substrate) for materials having useful properties.

Using the aforementioned dispenser systems, the reactants can be delivered to predefined regions on the substrate either sequentially or simultaneously. In a preferred embodiment, the reactants are simultaneously delivered to either a single predefined region on the substrate or, alternatively, to multiple predefined regions on the substrate. For example, using an ink-jet dispenser having two nozzles, two different reactants can be simultaneously delivered to a single predefined region on the substrate. Alternatively, using this same ink-jet dispenser, a reactant can be simultaneously delivered to two different predefined regions on the substrate. In this instance, the same reactant or, alternatively, two different reactants can be delivered. If the same reactant is delivered to both of the predefined regions, it can be delivered at either the same or different

concentrations. Similarly, using an ink-jet dispenser having eight nozzles, for example, eight different reactants can be simultaneously delivered to a single predefined region on the substrate or, alternatively, eight reactants (either the same or different) can be simultaneously delivered to eight different predefined regions on the substrate.

To deposit reactant droplets consistently at precisely specified regions using a dispenser, a frame of reference common to the delivery instrument and the substrate is required. In other words, the reference coordinates of the instrument must be accurately mapped (saving results, adjusting parameters) onto the reference coordinates of the substrate. Ideally, only two reference points on the substrate would be required to completely map the array of reaction regions. The dispenser instrument locates these reference points and then adjust its internal reference coordinates to provide the necessary mapping. After this, the dispenser can move a particular distance in a particular direction and be positioned directly over a known region. Of course, the dispenser instrument must provide precisely repeatable movements. Further, the individual regions of the array must not move with respect to the reference marks on the substrate after the reference marks have been formed. Unfortunately, pressing or other mechanical operations commonly encountered during fabrication and use of a substrate can warp the substrate such that the correspondence between the reference marks and the reaction regions is altered.

Starting at a single reference point, the micropipette or other dispenser is translated from one reaction region to other reaction regions of the substrate by a correct distance in the correct direction (this is the "dead reckoning" navigational

technique). Thus, the dispenser can move from region to region, dispensing correctly metered amounts of reactant. In order to initially locate the reference point and align the dispenser directly over it, a vision or blind system can be employed. In a vision system, a camera is rigidly mounted to the dispenser nozzle. When the camera locates the reference point(s), the dispenser is known to be a fixed distance and direction away from the point, and a frame of reference is established. Blind systems locate the reference point(s) by capacitive, resistive, or optical techniques, for example. In one example of an optical technique, a laser beam is transmitted through or reflected from the substrate. When the beam encounters a reference mark, a change in light intensity is detected by a sensor. Capacitive and resistive techniques are similarly applied. A sensor registers a change in capacitance or resistivity when a reference point is encountered.

The properties listed in Table I can be screened for using conventional methods and devices known to and used by those of skill in the art. Scanning systems which can be used to screen for the properties set forth in Table I include, but are not limited to, the following: scanning Raman spectroscopy; scanning NMR spectroscopy; scanning probe spectroscopy including, for example, surface potentialometry, tunnelling current, atomic force, acoustic microscopy, shearing-stress microscopy, ultra fast photo excitation, electrostatic force microscope, tunneling induced photo emission microscope, magnetic force microscope, microwave field-induced surface harmonic generation microscope, nonlinear alternating-current tunnelling microscopy, near-field scanning optical microscopy, inelastic electron tunneling spectrometer, etc.; optical

microscopy at different wavelengths; scanning optical ellipsometry (for measuring dielectric constant and multilayer film thickness); scanning Eddy-current microscope; electron (diffraction) microscope, etc.

Schultz et al. do not disclose that he dispensed liquid is detected "at" (as defined by applicant) respective locations on the substrate.

Bogen et al. disclose an automated slide stainer with slides mounted in a horizontal position on a rotary carousel. Reagents and rinse liquids are automatically dispensed onto tissue sections or cells mounted on slides for the purpose of performing chemical or immunohistochemical stains.

The device comprise a dispense sensor 95 is positioned underneath the bulk liquid dispensing port 68 to provide verification that liquid was dispensed when one of the solenoid valves 72a-72f were transiently opened. The dispense sensor 95 comprises an optical sensor and an LED light source. When liquid is dispensed from the bulk liquid dispensing port 68, the liquid interrupts the light beam. The change in resistance across the sensor as a result of the decrement in light intensity is communicated to the controller 86.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify method and the device of Schultz et al. to include the drop sensing element as taught by Bogen in order to allow for inventory of the fluid dispensed and monitor if the dispensers are functioning correctly.

Conclusion

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Brookes et al. disclose a device for scanning liquids.

Fsher and Hess et al. disclose arraying devices.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is (703) 305-0399. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 703-308-4037. The fax phone numbers for

the organization where this application or proceeding is assigned are (703) 872-9310 for regular communications and (703) 872-9311 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

brg
July 22, 2003

Jill Warden
Supervisory Patent Examiner
Technology Center 1700